

REMARKS:

The claims in the application are 34, 36-55, 57-60, 62-66 and Claims 67-74 added by the present amendment.

Favorable reconsideration of the application as amended is respectfully requested.

The amendment to independent Claims 34 and 53 herein finds support throughout the present application, e.g., on page 3 of the present application. The previously-pending claims have been amended to correspond with the amendments to independent Claims 34 and 53 while Claims 67 and 68 find support in Fig. 1; claims 69 and 70 find support in Table 3 on page 14 and in Fig. 2; Claims 71 and 72 find support in Table 4 at the top of page 16; and Claims 73 and 74 find support in Table 5 at the top of page 18 of the present application.

Accordingly, the only outstanding issue is the art rejection of the claims . More particularly, Claims 34-66 have been rejected under 35 U.S.C. §103 as obvious over European appln. no. 0956869 (an equivalent to U.S. patent no. 6,200,587 to Soe et al) in view of U.S. patent no. 4,340,731 to Columbo et al, U.S. patent no. 5,962,026 to Edwardson et al and U.S. patent no. 4,265,233 to Sugitachi et al. It is basically contended it is obvious to prepare a hemostatic composition containing carboxymethylated cellulose fiber taught by Columbo et al since Sugitachi et al teach such fiber in wound-healing context, Edwardson et al teach immobilizing a thrombin-like enzyme on supports with carbodiimide and EP '869 teaching preferred use of low-substituted carboxymethyl cellulose.

However, it is respectfully submitted the invention recited in all pending claims herein is patentable over the applied art for the following reasons.

The present invention provides clearly distinct and important improvement in manufacturing a soluble trauma-healing hemostatic cellulose fiber containing coagulation proteins and which rapidly dissolves when contacting blood to provide excellent hemostatic effect, especially in a large amount of blood such as a wound. More particularly, the claimed hemostatic fiber exhibits the important hemostatic effect in the following manner:

(1) The cellulose fiber possesses excellent absorption by tissue fluid such as blood and rapidly dissolves when contacting the blood;

(2) The cellulose fiber accelerates coagulation reaction of fibrin monomers converted from fibrinogen with thrombin which are contained in the soluble trauma-healing hemostatic cellulose fiber including coagulation proteins, also promoting and activating a blood clot cascade even when the blood clot cascade is low or inactive; and

(3) Cross-linking reaction of the coagulation factor XIII which is contained in the same soluble trauma-healing hemostatic cellulose fiber stabilizes the agglutinates.

Basically, the inventive hemostatic fiber possessing the above three important properties was discovered by finding the fiber enhances adhesion and aggregation of blood platelets at the wound and furthermore interacts with fibronectin which is an adhesion protein, to promote cell adhesion activity of the fibronectin. These features are explicitly documented in the demonstrative evidence presented in the various examples, tables and figures in the present application.

More particularly, the test results presented in Table 1 found at the bottom of page 9 of the present application document ability to control degree of hydroxyl group substitution in the hemostatic cellulose fiber, namely by controlling reaction time with monochloro acetic acid in accordance with the inventive method of preparation (please see, e.g., Claim 62). The results reported in Table 2 found at the top of page 12 of the specification document complete solubility of the inventive hemostatic cellulose fiber in water and saline, whether the coagulation protein is imparted to the fiber by spraying or chemical bonding. Test results presented in Fig. 1 show the substantial improvement in fibrinomer absorptivity with the inventive hemostatic fiber having the coagulation protein either applied to the surface thereof or chemically bonded thereto (graphs C and D); thus, the methods of application clearly result in a different improved hemostatic fiber being obtained are not mere processing limitations (please see, e.g., Claims 37 and 40).

The results presented in Table 3 on page 14 of the present application and illustrated in Fig 2 document improved platelet agglutination activity provided by the inventive hemostatic fiber. Table 4 at the top of page 16 documents greatly improved adhered cell count with the inventive fiber. Test results documented in Table 5 at the top of page 18 of the specification show hemostasis can be achieved with the inventive fiber in as little as 10-11 seconds.

Thus the claimed hemostatic fiber absorbs both blood and tissue fluid when applied to the trauma site, generating potent fibrin agglutinates under the action of the coagulation proteins and providing quick effect hemostasis by additionally assisting platelet adhesion and agglutination. The features of the presently claimed invention together with the accompanying advantages attained thereby are neither taught nor suggested by the applied art for the following reasons.

As pointed out the amendment of January 13, 2003, Soe et al., the U.S. equivalent to EP '869, fails to disclose a hemostatic fiber. The advantageous features of the claimed invention set forth under subheadings (1)-(3) supra, are neither taught nor suggested by EP '869. The subordinate references add nothing to the teachings of EP '869 for the following reasons.

Columbo et al merely relate to etherification of cellulose fibers ultimately used in products such as sanitary towels or napkins, bandages, tampons, etc (column 7, lines 1-2); there is no suggestion in this reference of utilizing the fibers for wound healing benefit. Edwardson et al just contain a general disclosure that a thrombin-like enzyme can be immobilized upon a support such as cellulose or derivatives; there is no explicit teaching in Edwardson et al of preparing an etherified cellulose fiber as in the claimed invention with the coagulation protein imparted in the inventive fashion.

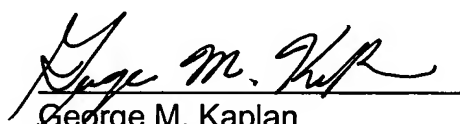
Finally, Sugitachi et al merely disclose fixing blood coagulation factor XIII to a variety of structures such as sutures, pads, bandages, etc. formed from a variety of materials, such as carboxymethylcellulose (column 1, line 49- column 2, line 5). There is no explicit suggestion in Sugitachi et al of preparing the claimed etherified cellulose fiber with all three coagulation proteins imparted thereto. The structures of Columbo et al and Sugitachi et al are not designed for dissolution as claimed; attention is called, e.g., to claims 45 and 47 which recite the claimed fibers can be pulverized before hemostatic application.

Accordingly, it is respectfully submitted the claimed invention and accompanying advantages as documented in the present application, are neither taught nor suggested by the applied art, even in combination. It is noted a combination of four references has been used to reject the claims in the Office Action. This, in and of itself, is evidence of the unobvious nature of the invention recited in the present application. Furthermore, the claims herein clearly recite features that are not contained in any of the references, e.g., the application of three coagulation proteins. It is again respectfully emphasized the test data extensively presented in the present application clearly documents the improved unobvious activity of the inventive fiber and preparation method claimed herein. The only explicit teaching of the claimed invention is found in the present application. Accordingly, any combination of art to reject the claims merely constitutes improper hindsight reconstruction of the claimed invention in light of the invention disclosure herein.

Accordingly, in view of the forgoing amendment and accompanying remarks, it is respectfully submitted all claims pending herein are in condition for allowance. Please contact the undersigned attorney should there be any questions. The requisite fee for the new claims introduced herein is enclosed.

Early favorable action is earnestly solicited.

Respectfully submitted,
DILWORTH & BARRESE

A handwritten signature in dark ink, appearing to read "George M. Kaplan", is written over a horizontal line.

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